REMARKS

Claims 10, 11 and 18-22 are withdrawn as per the Applicants' Election noted in the Response dated May 10, 2006. Applicant reserves the right to file further related applications addressing the subject matter of Groups II through VI inclusive. Amended Claims 12, 14, 15 and original Claims 1-9, 13, 16 and 17 remain in the application.

The Examiner has objected to Claims 12, 14 and 15 as depending on non-elected subject matter. Applicants have amended Claims 12, 14 and 15 to eliminate reference to non-elected Claim 11.

The Examiner has objected to Claims 14 and 15 under 37 CFR 1.75(c) as being in improper form as they were multiple dependent claims that depended on other multiple dependent claims. Applicants have amended Claims 14 and 15 to comply with 37 CFR 1.75(c) and therefore examination of Claims 14 and 15 on their merits is respectfully requested.

In paragraph 6 of the Office Action the Examiner has provisionally rejected Claims 1-9 and 12-17 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-2 and 6 of Guntoori *et al.* in the co-pending Application No. 11/099,624. While the Applicants agree that both processes are directed towards making the same compound, (R)- 5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]–5-hydroxy-3-oxo-1-heptanoic acid, tert-butylester, Applicants respectfully disagree with the Examiner that Claims 1, 2 and 6 of Guntoori *et al.*, which have since issued as US 7,112,604, render Claims 1-9 and 12-17 prima facie obvious.

Claim 1 of Guntoori *et al.* states:

> 1. The process for preparing (R)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-5-hydroxy-3-oxo-1-heptanoic acid, R-substituted ester 9 comprising:
>
> (a) making (R,S)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-3-hydroxy-1-pentanoic acid, (S)-2-hydroxy-1,2,2-triphenylethyl ester by reacting the aldehyde 1 with the enolate form of (S)-2-hydroxy-1,2,2-triphenylethyl acetate substituent in a chelating co-solvent;
>
> (b) hydrolysis of (R,S)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-3-hydroxy-1-pentanoic acid, (S)-2-hydroxy-1,2,2-triphenylethyl ester (2a and 2b) using a base, in a solvent to form the carboxylic acid 7;

(c) treating the acid 7 with a chiral base to form a salt and purifying the salt to obtain enantiomerically enriched (R)-7 chiral base salt;

(d) alkylation of the (R)-7 chiral base salt or the free base derived from (R)-7, forming (R)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-5-hydroxy-3-oxo-1-heptanoic acid, R-substituted ester 9 which would be useful in the production of atorvastatin calcium 6,

wherein R is C1 to C6 alkyl, C6 to C9 aryl or C7 to C10 aralkyl.

Thus, enhancement of the optical purity of acid 7 is required in the claimed process and is accomplished through the additional purification step (c) by the formation of a chiral base salt. Claims 2 and 6 of Guntoori *et al.* are dependent on Claim 1.

Claim 1 of the present application states:

1. A process for preparing (R)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-5-hydroxy-3-oxo-1-heptanoic acid, tert-butylester comprising:

(a) reduction of 5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-3-oxo-1-pentanoic acid, (R)-2-hydroxy-1,2,2-triphenylethyl ester

(b) hydrolysis of (R)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]–3-hydroxy-1-pentanoic acid, (R)-2-hydroxy-1,2,2-triphenylethyl ester using an alkali base in a solvent to form the acid;

(c) alkylation of the acid forming (R)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]–5-hydroxy-3-oxo-1-heptanoic acid, tert-butylester.

Claims 2-9 and 12-17 of the present application are dependent on Claim 1.

Applicants' process in Claim 1 is differentiated over Claim 1 of Guntoori *et al.* in that the increased optical purity of the final product is achieved through the reduction step. The stereoselectivity of this reduction step is such that further purification, such as that in step (c) of Guntoori *et al.* in, is not required. Nowhere in Guntoori *et al.* is there a reduction step, nor is there motivation in the Guntoori *et al.* specification for the skilled person to conduct such a step since the necessary ketone, required for a reduction, is not present in any of the compounds in Guntoori *et al.*

Similarly, such an approach is not contemplated within the specification of Guntoori *et al.* In Guntoori *et al.*, step (a) involves the formation of (R,S)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-3-hydroxy-1-pentanoic acid, (S)-2-hydroxy-1,2,2-triphenylethyl ester by reacting the aldehyde 1 with the enolate form of (S)-2-hydroxy-1,2,2-triphenylethyl acetate substituent in a chelating co-solvent; whereas in the present application in step (a) there is the

reduction of 5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-3-oxo-1-pentanoic acid, (R)-2-hydroxy-1,2,2-triphenylethyl ester.

Not only are the end products of each of Guntoori *et al.* and Applicant's step (a) different, but the chemistry is not the same.

Similarly, the hydrolysis step of Guntoori *et al.* (b) involves the hydrolysis of (R,S)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]-3-hydroxy-1-pentanoic acid, (S)-2-hydroxy-1,2,2-triphenylethyl ester (2a and 2b) using a base, in a solvent to form the carboxylic acid 7; whereas in the present application the hydrolysis of step (b) is of a completely different compound, namely (R)-5-[2-(4-fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]–3-hydroxy-1-pentanoic acid, (R)-2-hydroxy-1,2,2-triphenylethyl ester using an alkali base in a solvent to form the acid.

A side by side comparison of Claim 1 of each of Guntoori *et al.* and the present application is attached for the Examiner's convenience. Applicants assert that the processes in Guntoori *et al.* and the present application are each novel and non-obvious.

In the rejection on the basis of non-statutory obviousness-type double patenting, the Examiner has also cited Claims 2 and 6 of Guntoori *et al.* against Claims 1-9 and 12-17 of the present application. Applicants respectfully disagree with the Examiner since each of Claims 2 and 6 are dependent on the previously discussed Guntoori *et al.* Claim 1. Applicants having already asserted novelty and assert non-obvious over Guntoori *et al.* of Claim 1 for the previously discussed reasons. Furthermore, the same reasons discussed above apply to Claims 2-9 and 12-17 of the present application. Thus, Applicant respectfully submits the rejection of Claims 1-9 and 12-17 as being unpatentable over Claims 1, 2 and 6 of Guntoori *et al.* on the basis of the judicially created doctrine of obviousness-type double patenting is overcome.

If the Examiner has any questions, the Examiner is respectfully requested to contact Applicants' Agent, Marcelo K. Sarkis at (905) 771-6414 collect at the Examiner's convenience.

Respectfully submitted,

IVOR M. HUGHES

Marcelo K. Sarkis
Registration No. 37015
Agent for the Applicant

MKS*kdk
Enclosures
1. Requisition for 1 Month Extension of Time
2. Check for $120.00 U.S
3. Claim comparison